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ORIGINAL ARTICLE

Appendiceal diverticular disease

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Summary *Introduction:* As a rule, diverticulosis of the appendix is identified incidentally during a pathological examination after an appendectomy. The disease is rare and easily ignored. Only one case has been reported in Taiwan.
Aim: In this study, we retrospectively reviewed the medical records of patients who had undergone appendectomy at the Ton Yen General Hospital, a local hospital in Taiwan.
Methods: From June 2004 to May 2012, 10 patients with appendiceal diverticulosis were documented. Their clinical presentations, laboratory data, and pathological characteristics were analyzed.
Results: All patients were diagnosed after their operations. The incidence rate was 0.88% (10/1131). The patients comprised eight men and two women. The age distribution was 22—71 years with an average of 39.2 years. All diverticula were acquired, not congenital. Eight patients presented with acute appendicitis and diverticulitis, one patient presented with a normal appendix and acute diverticulitis, and one patient presented with periappendicitis with a noninflammatory diverticulum. Three patients also presented with mucoceles, one patient with a hyperplastic polyp, and two patients had a severe case of inflammation with epithelial regenerative atypia and mild dysplasia. The number of diverticula for each patient ranged from one to six. Multiple diverticula were present in 80% of the patients. In 90% of the patients, the diverticula were located in the distal portion of the appendix. Perforation was noted in seven (70%) patients.
Conclusion: The diverticula could have been preoperatively diagnosed with careful differentiation of the clinical presentations. High-resolution ultrasound or CT scans may facilitate diagnosis. The recommended treatment for asymptomatic appendiceal diverticulosis is

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prophylactic appendectomy because of the high perforation rate and a significant association with neoplasia. Once a surgical specimen is obtained, we advise conducting a thorough pathologic examination and securing additional sections to identify a greater number of diverticula, perforations, and associated neoplasms.

1. Introduction

Appendiceal diverticulosis is a rare disease and a diagnosis of the disease is easily missed. Only one case has been reported in Taiwan.[1] The clinical presentations of acute appendicitis and appendiceal diverticulum disease are extremely similar; however, a number of differences can be observed.[2] Most cases of appendiceal diverticular disease are incidentally identified during an operation or pathological examination.[2–4] Diagnosing appendiceal diverticulosis preoperatively is difficult. In this retrospective study, we present 10 cases of appendiceal diverticulosis. We analyzed the clinical features, laboratory data, and pathological findings of each case. We also compared the clinical manifestations of typical acute appendicitis and appendiceal diverticulitis to help identify the differences.

2. Materials and methods

We retrospectively reviewed the medical records of patients who had undergone an appendectomy at a local hospital (Ton Yen General Hospital, Taiwan) from June 2004 to May 2012. Ten patients with appendiceal diverticulosis were documented. The clinical presentations were recorded and included pain location, duration, the number of admissions before the operation, and days of hospitalization. The patients' imaging data, whether they had a preoperative fever, and laboratory data were reviewed. The laboratory data included a white blood cell count, neutrophil percentage, and C-reactive protein (CRP) level. For the pathological examination, two transverse sections of the proximal cut end, the middle portion, and one longitudinal section of the tip of the appendix (including the distal portion) were obtained as the standard sampling procedure. When one protruding pouch was detected, additional transverse sections were taken. Fig. 1 is a photograph of one patient's appendiceal diverticula. The appendiceal diverticula were microscopically categorized as congenital or acquired diverticula.

Congenital diverticula (also called true diverticula) are composed of the following four layers: (1) mucosa (including the muscularis mucosa); (2) submucosa; (3) muscularis propria; and (4) serosa. Acquired diverticula (also called pseudodiverticula) lack the muscularis propria. Appendiceal diverticular diseases are also classified into four main subtypes. Type 1 is diverticulitis with a normal appendix; Type 2 is diverticulitis with appendicitis; Type 3 is a noninflamed diverticulum with appendicitis; and Type 4 is a noninflamed diverticulum with a normal appendix. The microscopic definition of appendicitis is neutrophil infiltration into the muscle layer, and the microscopic definition of appendiceal diverticulitis is neutrophil infiltration into the mucosal and submucosal layers of the diverticula. Microscopic diverticular perforation is defined as ulceration of the diverticular mucosal layer, destruction of the muscularis mucosa, and suppurative inflammation of the serosal layer with or without a foreign body reaction. The diverticulum location, number, maximal size, pathological diagnosis, and subtype were analyzed.

3. Results

In our hospital (TYGH), the incidence of appendiceal diverticulosis was 0.88% (10/1131) in the appendectomy specimens. The patients consisted of eight men and two women. The mean age of the patients was 39.2 years and ranged from 22 years to 71 years. Tables 1 and 2 list the patients' clinical presentation and laboratory data, respectively. The patients' white blood cell (WBC) count ranged from 9860 /μL to 23,790/μL. The neutrophil percentages ranged between 60% and 85%. The C-reactive protein (CRP) values ranged from 0.02 mg/dL to 17.86 mg/dL. The duration of hospitalization ranged from 2 days to 6 days. Three patients developed a preoperative fever (i.e., a body temperature of 38°C or greater). All patients who experienced a fever had perforated diverticulitis. One patient (Case 9) who presented with a normal appendix and diverticulum had a high CRP level; however, his WBC count was not elevated and he did not develop a fever.

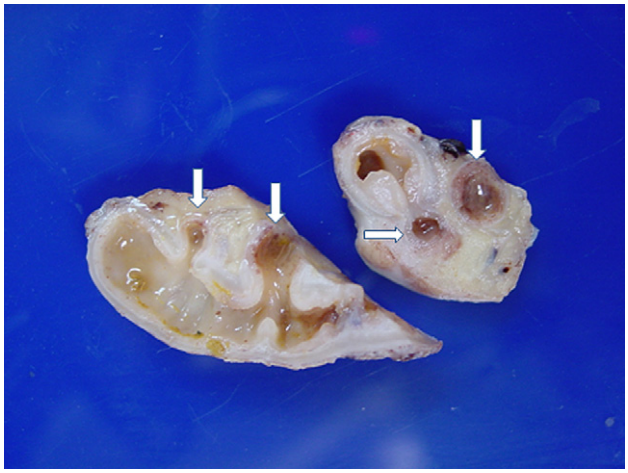

Figure 1 Sections of the appendix of Patient 6. The longitudinal section of the distal portion of the appendix is on the left side. The transverse section of the middle portion of the appendix is on the right side. The white arrows indicate the diverticula.

Table 1 The clinical presentations of the patients.

Patient no.	Sex	Age	Symptom	Symptom duration	Number of admissions before the operation	Days of hospitalization
1	M	41	RLQ pain	<1 d	1	4
2	M	36	Periumbilical RLQ pain	2 d	2	2
3	M	36	RLQ pain	<1 d	1	4
4	M	29	Abdominal discomfort	4–5 d	1	6
5	M	42	RLQ pain	2 d	1	3
6	M	49	RLQ pain	<1 d	1	3
7	M	22	Abdominal discomfort	4 d	1	5
8	M	41	RLQ pain	<1 d	1	4
9	F	71	RLQ pain	<1 d	2	3
10	F	25	RLQ pain	<6 h	1	4

RLQ = right lower quadrant.

Five of the patients (Cases 1, 3, 4, 5, and 8) underwent a computed tomography (CT) scan. The CT image findings showed abnormal swelling, edematous changes, phlegmonous reaction, increased transverse diameter of the appendix with perifocal infiltration, and an appendicolith. However, in none of the patients was appendiceal diverticulosis suggested.

The appendices and mesoappendices in these patients typically formed inflammatory masses or phlegmons covered by pus. The longitudinal length and the transverse diameter of the masses ranged 5–7 cm and 0.8–4 cm, respectively. The diverticula were typically found along the mesenteric border of the mesoappendix. The number of diverticula ranged from one to six in each patient. Multiple diverticula were observed in eight (80%) patients. The diverticula were located at the tip or distal portion of the appendix in nine patients, and located in the middle portion of the appendix in six patients. The maximum diameter of the diverticula ranged from 0.3 cm to 0.8 cm.

In the 10 appendices, all diverticula were acquired without the muscularis propria. Eight patients (Cases 1–7 and 9) presented with acute appendicitis and diverticulitis. The diverticular lumens contained mucus, pus, or fecaliths. Three patients (Cases 2, 6, and 7) exhibited dilated appendiceal lumens that were filled with mucus (i.e., mucoceles). Five appendiceal lumens contained feces, and five contained pus. In the inflammatory foci, the mucosa showed reactive epithelial proliferation with pseudostratification of epithelial cells, increased mitotic activity, and distortion of the glandular architecture. Patients 1 and 9 presented with marked inflammation, epithelial regenerative atypia, and small foci of adenomatous change with mild dysplasia. Patient 8 had a normal appendix with mild periappendicitis and a single noninflamed diverticulum with an undilated appendiceal cavity. This diverticulum contained a fecalith and was located in the middle portion of the appendix. There was a small focus containing a hyperplastic polyp over the appendiceal mucosa; it measured 1 mm. Patient 10 had a normal appendix and acute diverticulitis in one of two diverticula. A fecalith in the appendiceal lumen and adipocyte infiltration in the appendiceal submucosa were also present. Perforation occurred in 70% (7/10) of the patients. The patients with multiple diverticula had higher perforation rates than patients with a single diverticulum (75% [6/8] patients vs. 50% [1/2] patients). The perforation rate however was not correlated with the diverticular size. Table 3 lists the pathological findings of the 10 patients.

Table 2 The laboratory data of the patients.

Patient no.	WBC count (cells/μL)	Neutrophil (%)	CRP (mg/dL)	Preoperative fever
1	14820	78	0.15	No
2	11160	70.7	0.286	No
3	23790	83	0.646	Yes
4	11890	67.4	3.648	No
5	16240	85	4.268	No
6	9930	65.3	NA	Yes
7	18080	60	17.086	No
8	9860	79.1	3.76	No
9	8000	68.3	NA	Yes
10	13980	84.3	0.02	No

The normal range for the WBC count is 3900–10 600/μl; for the neutrophil percentage, 45–75%; and for the CRP, less than 0.5 mg/dL. CRP = C-reactive protein; NA = not available; WBC = white blood cell.

Table 3 The pathological characteristics of the patients.

Patient no.	Pathology diagnosis	Diverticulum, subtype	Diverticulum perforation	Diverticulum location	Number of diverticula	Diverticulum size (maximal)	Dilatation of appendix cavity
1	Mild A + D	Acquired, 2	Yes	Near tip	2	0.4 cm	No
2	A + D	Acquired, 2	Yes	Middle and near tip	6	0.5 cm	Yes
3	A + D	Acquired, 2	Yes	Middle and near tip	3	0.4 cm	No
4	A + mild D	Acquired, 2	No	Tip	2	0.8 cm	No
5	Mild A + D	Acquired, 2	Yes	Middle and near tip	5	0.5 cm	No
6	A + D	Acquired, 2	Yes	Middle and near tip	5	0.5 cm	Yes
7	A + D	Acquired, 2	Yes	Near tip	2	0.3 cm	Yes
8	NA + diverticulum	Acquired, 4	No	Middle	1	0.6 cm	No
9	A + D	Acquired, 2	Yes	Near tip	1	0.5 cm	No
10	NA + D	Acquired, 1	No	Middle and near tip	2	0.6 cm	No

A = acute appendicitis; D = acute diverticulitis; NA = normal appendix.

4. Discussion

The incidence of appendiceal diverticulosis is 0.004–2.1% in appendectomy specimens[1–3] and 0.2–0.66% in autopsy cases.[2,4] Appendiceal diverticula are traditionally categorized as true diverticula or pseudodiverticula. True diverticula are congenital and are composed of the following four layers: (1) mucosa (including the muscularis mucosa); (2) submucosa; (3) muscularis propria; and (4) serosa. Pseudodiverticula are acquired and lack the muscularis propria. Most clinical cases of diverticula are of the acquired type.[1,3] Congenital diverticula are extremely rare; less than 50 cases have been reported. Thus, the incidence of congenital diverticula is approximately 0.014% in appendectomy specimens.[2] Congenital diverticulosis accounts for approximately 3% of all cases of appendiceal diverticular disease.[2] The mean age of patients presenting with congenital diverticulosis is 31 years and the mean age of patients presenting with acquired diverticulosis is 37–39 years.[2] Multiple diverticula are present in patients with acquired diverticulosis, whereas only one diverticulum has ever been identified in people with congenital diverticulosis.[2] Perforation of acquired diverticula occurs quite easily (in up to 66% of cases) because of the lack of the muscularis propria layer.[2] By contrast, congenital diverticula have a thick muscle layer (i.e., the muscularis propria) and therefore they are not perforated easily (perforation occurs in only 6.6% of cases). Table 4 lists the differences between congenital and acquired diverticula.

In our case series, the incidence rate was 0.88%. All 10 patients had acquired diverticula, and the mean patient age was 39.2 years. Our results are similar to those reported in the medical literature.[2] Eight of 10 patients had multiple diverticula, and seven patients presented with diverticular perforation. The perforation rate was 70% in our series and 27–66% in a review by Abdullgraffar.[2]

On examining the pathogenesis of congenital diverticula, Favara et al. found that trisomy 13–15 affected seven of eight congenital diverticulum patients.[4] This suggests the importance of genetic or chromosomal factors. Other possible mechanisms include failed recanalization of the appendiceal lumen, duplication of the appendix, remnants of epithelial inclusion cysts in the appendiceal wall, failed obliteration of the vitelline duct, and wall traction caused by adhesions.[4] Hypotheses on the development of acquired diverticula advocate either inflammatory causes or advocate noninflammatory causes. The inflammation hypothesis states that several episodes of inflammation or infection lead to atrophy of lymphoid tissues, resulting in a weaker and thinner residual wall.[2] The noninflammation hypothesis holds that increased intraluminal pressure causes acquired diverticula to develop.[2] The combination of luminal obstruction and muscular contractions drive this development. Secondary obstructions after inflammation, stricture, fecaliths, and tumors cause increases in muscular activity and luminal pressure.[2] Nearly 60% of diverticula are located in the distal third of the appendix.[4] For our 10 patients, the diverticula were distributed over 90% of the distal portion and over 60% of the middle third of the appendix. Eight patients presented with acute diverticulitis and appendicitis. Three patients had dilated appendiceal lumens. Five appendiceal lumens contained feces or fecaliths, and five appendiceal lumens contained pus. This finding would support the hypotheses on the inflammatory or noninflammatory causes of acquired diverticula.

Several risk factors are associated with acquired appendiceal diverticulosis. These include male sex, an age

Table 4 Differences between true diverticula and pseudodiverticula.

	Mechanism	Perforation rate	Diverticulum percentage	Mean age	Histology structure	Diverticulum number
True	Congenital	Low	3%	31 y	Four layers	Single
Pseudo	Acquired	High	97%	37–39 y	Three layers	Multiple

older than 30 years, and a diagnosis of Hirschsprung's disease or cystic fibrosis.[1,3] Patients are typically diagnosed with cystic fibrosis at adolescence (on average at 13 years) and have up to a 14% incidence of acquired appendiceal diverticulosis.[2] Appendiceal diverticulosis is unrelated to colonic diverticulosis, and therefore their pathogeneses may differ. We reviewed the medical histories and image studies of each of the 10 patients and found no evidence of colonic diverticula.

Appendiceal diverticular diseases are typically classified into 4 main subtypes. Type 1 is diverticulitis with a normal appendix; Type 2 is diverticulitis with appendicitis; Type 3 is a noninflamed diverticulum with appendicitis; and Type 4 is a noninflamed diverticulum with a normal appendix. Type 1 is the most common of the four types.[1–3] However, among the 10 patients examined in this study, 8 patients had Type 2, only one patient had Type 1, and one patient had Type 4. In two of the eight patients with Type 2, a few neutrophils were identified in the muscularis propria adjacent to the acute inflammatory diverticulum. Thus, Type 2 may represent late-stage Type 1 or Type 3. Patients with Type 2 appendiceal diverticulitis were frequently symptomatic, which may increase the risk of perforation.

Three studies have indicated that appendiceal neoplasia is significantly associated with diverticular disease.[6–8] In a 23-case series reported by Dupre et al[6] in 2008, 11 (48%) patients with acquired diverticulosis also exhibited primary appendiceal neoplasia, which included five well-differentiated neuroendocrine tumors (i.e., carcinoids), three mucinous adenomas, one tubular adenoma, and two adenocarcinomas. In 1998, Medlicott and Urbanski[7] reported that 29% (9/31) of patients with acquired diverticulosis also had primary appendiceal epithelial neoplasia (7 adenomas and 2 goblet cell carcinoids). Lamps found that 42% (8/19) appendiceal low-grade mucinous neoplasms were associated with appendiceal diverticula.[8] In our case series of 10 patients, three patients had mucoceles, one patient had a small hyperplastic polyp, and two patients had epithelial regenerative atypia and small foci of adenomatous change with mild dysplasia.

Appendiceal diverticulosis is typically asymptomatic. The mechanism of symptomatic appendiceal diverticulosis is unknown.[5] Appendiceal diverticulitis is generally caused by partial or complete obstruction of the appendiceal lumen. Right lower quadrant abdominal pain subsequently develops.

Distinguishing appendiceal diverticulitis from acute appendicitis is difficult; however, several differences have been observed. Compared to the symptoms of appendicitis, symptomatic appendiceal diverticulitis has a longer duration of pain (1—14 days); primarily develops in older adults (older than 30 years); has a lower frequency of accompanying abdominal pain, nausea, and vomiting; and has a greater occurrence of right lower quadrant abdominal pain.[2,3] Table 5 lists the differences between the clinical manifestations of typical acute appendicitis and appendiceal diverticulitis.[2]

Image studies may facilitate preoperative diagnosis. Place reported the findings of an abdominal CT scan in a patient with appendiceal diverticulitis.[4] The scan showed a large pericecal phlegmon. However, CT image findings (e.g., appendiceal swelling, pericecal inflammation, abscess, phlegmon, and increased pericecal fat density) did not sufficiently distinguish appendiceal diverticulitis from cecal diverticulitis or appendicitis.[4] Kubota et al reported a patient who was diagnosed preoperatively by an abdominal ultrasound, which showed an enlarged, swollen appendix with a cross-section diameter of 10 mm and multiple small hypoechoic lateral pouchlike projections.[9] In the future, high-resolution ultrasound or CT scans may facilitate the preoperative diagnosis of appendiceal diverticulosis. Appendiceal diverticulosis may also be identified by surgeons during an operation if the distal portion of the specimen is longitudinally bisected along the long axis and the mesoappendiceal plane. We recommend that a frozen section study should be performed for suspected cases of appendiceal diverticulosis. However, most cases were incidentally identified during pathological examinations. Careful inspection and obtaining a greater number of serial sections are recommended when lesions are observed; this may enable identification of additional diverticula, perforation, or neoplasms.

For symptomatic appendiceal diverticulitis, an appendectomy is the optimal treatment. Regarding whether patients without symptoms require an appendectomy, most surgeons suggest a prophylactic appendectomy because, even in symptomless patients, the risk of perforation and mortality is higher in these patients than it is in the general population.[2] The perforation rate of appendiceal diverticulitis is four times higher than the perforation rate of acute appendicitis.[2] The mortality rate is 30 times higher in patients with perforated appendiceal diverticulitis than in patients with uncomplicated appendicitis.[2] For the 10 patients examined in this study, the perforation rate was 70%, and all perforations occurred in the diverticula. This finding supports previous observations. Laparoscopic

Table 5 Differences between clinical manifestations of typical acute appendicitis and appendiceal diverticulitis.

Clinical manifestation	Typical acute appendicitis	Appendiceal diverticulitis
Duration of symptoms	Short (24—48 h)	Long (days to years)
Age group	Young (19—20 y)	Old (37—39 y)
Character of pain	Acute, persistent	Chronic, intermittent
Attacks of RLQ pain	First time	Several times
Nausea and vomiting	Frequent	Seldom
Refer pain	Frequent	Seldom
Perforation rate	Low (6.6%)	High (27—66%)
Association with neoplasm	Rare	Frequent (29—48%)

RLQ = right lower quadrant.

appendectomy is considered a safe and appropriate treatment for uncomplicated appendiceal diverticulitis.[2]

In conclusion, appendiceal diverticulosis is a rare condition that is easily missed in preoperative and postoperative examinations. The clinical presentations of appendiceal diverticulitis and acute appendicitis are very similar and must be differentiated carefully. High-resolution imaging may facilitate the preoperative diagnosis of appendiceal diverticulosis. The recommended treatment for asymptomatic appendiceal diverticulosis is a prophylactic appendectomy because of the high perforation rate and a significant association with neoplasia. We advise conducting thorough pathologic examinations and obtaining additional sections to identify a greater number of diverticula, perforations, and associated neoplasms.

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